

## CHAPTER 14

### DERMATOLOGIC EVALUATION

#### INTRODUCTION

##### Background

The skin is a major target organ following heavy exposure to chlorophenols and dioxin and, therefore, is a primary focus of the Air Force Health Study (AFHS) clinical examination.

Since the association between chlorinated chemicals and chloracne was first noted in 1957,<sup>1,2</sup> a variety of animal experiments have shown the dermal sensitivity of rabbits, monkeys, and hairless mice to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,4,5-T (contaminated with TCDD), and other chlorinated dibenzo compounds, furans, or their brominated analogs.<sup>1-9</sup> Chloracne is not associated with exposure to 2,4-D.<sup>8</sup> Studies in animals have found the development of severe skin lesions in rats from 2,4-D exposure,<sup>9</sup> chloracne in hairless mice from TCDD that also causes an increase in synthesis of keratins,<sup>10</sup> and squamous cell carcinomas on the skin of the facial region in hamsters that had ingested TCDD.<sup>11</sup> One study in rats investigating testosterone interaction with TCDD has indicated that chloracne, hirsutism, and skin hyperpigmentation may result from the involvement of the endocrine system.<sup>12</sup> Accidental exposure to waste oils containing TCDD has caused significant dermal symptoms, including loss of hair, ulcerative dermatitis, and inflamed mucous membranes in horses, dogs, cats, and mice.<sup>13,14</sup> Studies have suggested that the chloracnogens induce a series of pathological skin changes in target cells of the epithelial lining of sebaceous glands via the Ah receptor.<sup>15</sup> Hyperkeratinization of these cells eventually leads to the formation of the comedone characteristic of acne.

The findings with animals have led to a number of studies with human epidermal cells to investigate the exact nature of TCDD skin effects in man. Skin effects generally recognized and investigated in man include: acanthosis (thickening of the epidermis), hyperkeratosis, and squamous metaplasia of the epithelial lining of the sebaceous glands.<sup>16</sup> Two studies found that TCDD produced hyperkeratinization, probably due to action in the epidermal basal cells to enhance terminal differentiation through the mechanisms regulated partly by Ah receptors.<sup>16,17</sup> (Another study in mice found that physiological factors beyond the epidermal cells may be involved in epidermal responses.<sup>18,19</sup>) Chloracne is believed to develop as hair follicles dilate and fill with keratin and the sebaceous glands become cystic.<sup>20</sup>

In humans, development of the hallmark rash, chloracne, is generally acknowledged to represent substantial topical or systemic exposure to one or more chloracnogens.<sup>1,3,6,21-27</sup> Acute fulminant chloracne is characterized by a maculopapular rash of active comedones, conforming to an eyeglass or facial butterfly distribution, often accompanied by chest, back, or eyelid lesions.<sup>3,27</sup> Since these lesions are seen in other skin diseases, the clinical diagnosis of chloracne is often based on a history of exposure to known acnegenic chemicals; however, the only definitive method of diagnosis is by histologic examination of biopsy material.<sup>27</sup>

Chronic chloracne has been clinically observed more than 30 years after onset,<sup>25</sup> but a biopsy is often necessary to confirm these cases.<sup>27</sup> Mild or transient cases of chloracne may be confused with persistent adolescent acne or other skin conditions.

The severity of the chloracne appears to be generally dose related, but may also depend on the route of administration, age, genetic predisposition, and the existence of acne vulgaris or other skin disorders.<sup>5,24,27</sup> Occasionally, exposure, via contaminated clothes of an industrial worker, has been associated with chloracne in family members.<sup>28</sup> Sequelae from severe chloracne include actinic elastosis, acne scars, disfigurement, excessive hair growth, and Peyronie's disease.<sup>5,25</sup> Severe chloracne is often accompanied by acute effects in other organ systems. In contrast, low to moderate exposure to chloracnegens generally produces mild chloracne with few, if any, attendant systemic signs and symptoms.

As noted in the AFHS Baseline Morbidity Report, over one-half of the veteran complaints in the Veterans Administration Herbicide Registry involved dermatologic conditions, a fact sometimes alluded to as "evidence" of exposure to Agent Orange. In actuality, skin disease was a major medical problem among American troops serving in Vietnam. Forty-seven percent of the combat-days lost in the 9th Infantry Division from July 1968 to June 1969 were due to dermatologic conditions.<sup>29</sup> These diseases were directly related to the tropical climate and terrain. Only in rare cases has the Veterans Administration made a diagnosis of chloracne in a Vietnam combat veteran. The natural history of chloracne suggests that most cases should have been diagnosed while in Vietnam, but a dermatologic survey failed to reveal any cases.<sup>29</sup> In a study of members of the American Legion, investigators found an increase in reports of skin rashes with blisters and changes in skin color among 102 men who reported having worked with herbicides in Vietnam.<sup>30</sup> Medical examinations to substantiate these reported problems were not conducted.

Most recognized chloracne cases have been diagnosed in chemical plant workers or in victims of industrial accidents. Thousands of cases were recorded in the 1930-1940 era, and earlier descriptions of chloracne-like disease were found between 1897 and 1901.<sup>31</sup> Industrial exposure to chloracnegens has been generally characterized as moderate-prolonged or severe-acute. In the setting of casual-sporadic exposure, as in the typical cases of the contaminated housing areas in Times Beach, Missouri, and the Quail Run Trailer Park, chloracne is virtually unknown.<sup>32-34</sup>

In the case of population exposures in Seveso, Italy, chloracne has been found in both children and adults.<sup>35-37</sup> A study comparing body burdens of the exposed adults in Seveso with dermally exposed prisoners who developed severe chloracne indicated body burdens in the Seveso population at 180 times that of the normal unexposed population and body burdens in the prisoners at 38 times that of the exposed Seveso population.<sup>38</sup> Another study of six factory workers with chloracne found adipose tissue levels of TCDD 15 times higher than normal population levels.<sup>39</sup> A study of farmers dermally exposed to 2,4-D pesticides found indications of dermal uptake but no skin effects,<sup>40</sup> indicating that 2,4-D does not act the same as TCDD on the skin in man. Workers at a 2,4,5-T (trichlorophenoxyacetic acid) plant were monitored for many years after their exposures; TCDD is a contaminant of 2,4,5-T.<sup>41</sup>

Eighty-six percent of the persons exposed during both normal operations and following an accident developed chloracne, and 52.7 percent still had it 20 to 30 years after the initial exposure. No other effects were found.

The use of chloracne as an indicator of TCDD exposure is still controversial. Yet many population studies use it without comment. Others have used it with qualifiers as to the possible existence of other initiators. Based on chloracne data an exposure limit of 200 pg/m<sup>3</sup> has been recommended; this level has been proposed to prevent chloracne from repeated acute exposures as well as chronic exposures. In the recommendation, it is believed that control of chloracne will prevent all other exposure effects.

A number of dioxin morbidity studies have shown a clustering of abnormal laboratory tests in individuals with chloracne. This has led some investigators to believe that long-term sequelae to dioxin exposure will be found only in people with chloracne. Other investigators feel that this belief is not consistent with normal spectrum-of-illness concepts and that effects may occur in the absence of chloracne.

### Baseline Summary Results

The 1982 Baseline clinical examination revealed an unexpected significant excess ( $p=0.03$ ) of basal cell carcinoma in the Ranch Hand group. Risk factor data (e.g., sun exposure, host factors of tannability, complexion) were not collected in 1982.

The 1982 examination focused on the diagnosis of chloracne both in historical terms by a detailed questionnaire and in contemporary terms via a comprehensive clinical assessment. The questionnaire data did not demonstrate anatomic, incidence, or onset-time patterns of acne in the Ranch Hand group that might support an inference of past chloracne, nor did the physical examination detect a single case. Fourteen biopsies from 11 participants also failed to document a chloracne diagnosis. A dermatology index (the number of clinically detected skin abnormalities per individual) was virtually identical between the Ranch Hand and Comparison groups, and was associated with the history of past acne in both groups. No exposure level associations were noted in any occupational category of the Ranch Hand group. The comprehensive dermatologic assessment did not reveal evidence of past or current chloracne in the Ranch Hand group.

### 1985 Followup Study Summary Results

Questionnaire data recaptured many of the acne parameters of the 1982 questionnaire, and the physical examination parameters were similar to the 1982 Baseline examination. Particular emphasis was given to the diagnosis of basal cell carcinoma and to the collection of risk factor data, e.g., skin color, reaction to sun, ethnicity (see Chapter 10, Malignancy).

Interval questionnaire data on the occurrence, time, and location of acne were analyzed to assess the possible historical diagnosis of chloracne. No significant difference was observed between groups for reported occurrence of acne, although the Ranch Hand cohort reported slightly more acne. The

occurrence of acne relative to 1961 was comparable between groups. A marginally significant difference in the occurrence of post-1961 acne was found, with more Ranch Hands than Comparisons reporting acne strictly post-Southeast Asia (SEA). The duration of post-1961 acne was not significantly different between the two groups.

For participants with post-SEA acne, the spatial eyeglass distribution of acne (suggesting chloracne) was observed to be similar for the Ranch Hand and Comparison groups, both for individual sites and the combination of acne on the eyelids, ears, and temples. This analysis suggested that the occurrence of skin disease compatible with chloracne was not different in the two groups.

Analyses of the 1985 followup physical examination data, as with the Baseline examination, placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. Secondary emphasis was given to 16 other minor conditions (generally not associated with chloracne) recorded at the physical examination.

No significant difference was found for any of these variables in the unadjusted analyses. The variable consisting of the 16 secondary conditions, labeled "other abnormalities," had the largest difference in the prevalence of abnormalities for the Ranch Hand cohort over the Comparison group, but the difference was nonsignificant. The covariate effects of age, race, occupation, and the presence of pre-SEA acne were often profound with respect to the recorded dermatologic conditions.

The adjusted analyses closely mirrored the unadjusted analyses, with no significance noted between groups for any variable. Only one group-by-covariate interaction was observed in the adjusted analysis of the dermatology index, with a group-by-presence of pre-SEA acne interaction noted. However, further analysis of this interaction did not show an adverse effect in the Ranch Hand group.

Exposure index analyses did support dose-response relationships for some of the variables in certain occupational strata, but did not reveal a strong pattern of results suggesting a relationship between skin disease and herbicide exposure.

Overall, the 1985 followup examination results paralleled the Baseline findings. Although the followup examination detected more dermatologic abnormalities than those present at Baseline, slightly more abnormalities were found in the Comparisons, and most relative risks approached unity. The longitudinal analysis for the dermatology index showed no statistically significant differences between groups in the change in results from the Baseline to the 1985 followup examination.

In conclusion, none of the questionnaire results disclosed an increased likelihood of past chloracne in the Ranch Hands. The physical examination did not diagnose a current case of chloracne. The dermatologic data were similar between the Ranch Hand and Comparison groups, and the longitudinal analysis of the dermatology index suggested equivalence between the Baseline and 1985 followup examination results.

## Parameters of the 1987 Dermatologic Evaluation

### **Dependent Variables**

The dermatologic evaluation was based on questionnaire and physical examination data.

### Questionnaire Data

During the face-to-face health interview, each study participant was asked about the occurrences of acne since the date of the last health interview. This self-reported information was used to update the reported acne data through the 1985 followup, which include date of occurrence, length of occurrence, and location for each occurrence. The variables defined below were constructed from the self-reported acne data and analyzed in the dermatologic evaluation.

- **Occurrence of Acne (Lifetime):**

Yes: at least one occurrence of acne

No: no occurrences of acne

- **Occurrence of Acne (Relative to SEA Tour of Duty):**

Post-SEA: all occurrences after the start of the first SEA tour

Pre- and post-SEA: multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour

Pre-SEA: last occurrence before the start of the first SEA tour

None: no occurrences of acne

- **Duration of Acne:** for (a) participants with all occurrences after the start of the first SEA tour (post-SEA) and (b) participants with all occurrences after the start of the first SEA tour or with multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA)

Computed as the sum of the length of occurrences in years; time periods were only counted once in the case of occurrences in overlapping time periods; occurrences of less than a month were counted as 1 month

- **Location of Acne:** for (a) participants with all occurrences after the start of the first SEA tour (post-SEA) and (b) participants with all occurrences after the start of the first SEA tour or with multiple occurrences, both before and after the start of the first

SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA)

Locations: temples; eyes/eyelids; ears; temples and eyes; eyes and ears; temples and ears; temples, eyes, and ears; and other sites (cheeks, nose, forehead, jaw/chin, chest, back)

If more than one episode of acne occurred, cases involving the temples, eyes, or ears took precedence; multiple-site involvement took precedence over single-site involvement.

The analysis of occurrence of acne was based on responses from all of the participants of the 1987 followup. The occurrence of acne relative to SEA tour of duty was analyzed using all of the participants of the 1987 followup, all participants excluding those with both pre- and post-SEA acne, and all participants of the 1987 followup stratified by pre-SEA occurrence (yes/no) of acne. Duration of acne and location of acne were both analyzed twice. In one case, the location of acne was limited to the participants who had all occurrences after the start of the first SEA tour (post-SEA). The second analysis was based on the participants who had all occurrences after the start of the first SEA tour or who had multiple occurrences, both before and after the start of the first SEA tour, or a case of acne that began before the start of the first SEA tour and that ended after starting the SEA tour (post-SEA combined with pre- and post-SEA).

Duration of acne was analyzed as a continuous variable. The other variables are discrete.

No participants were excluded for medical reasons from the analysis of these variables.

The information on biopsies was tabulated. Further description on the analysis of the biopsy data is presented in Chapter 10, Malignancy.

#### Physical Examination Data

Eight variables from the physical examination data were analyzed in the dermatologic evaluation. The variables were comedones, acneiform lesions, acneiform scars, depigmentation, inclusion cysts, hyperpigmentation, other abnormalities, and dermatology index. The variable, other abnormalities, was coded as normal/abnormal. A participant was considered as abnormal for this variable if any of the following disorders were detected in the physical examination: jaundice, spider angiomas, palmar erythema, suspected melanoma, palmar keratoses, actinic keratoses, petechiae, ecchymoses, conjunctival abnormality, oral mucosal abnormality, fingernail abnormality, toenail abnormality, dermatographia, cutis rhomboidalis, suspected basal cell carcinoma, suspected squamous cell carcinoma, nevus, or other abnormalities. The dermatology index was formed by counting the number of abnormalities present for the following conditions: comedones, acneiform lesions, acneiform scars, and inclusion cysts. All other variables were coded as yes/no.

No participants were excluded for medical reasons from the analysis of these variables.

### **Covariates**

No adjustments were made in the analysis of occurrence of acne. Presence of pre-SEA acne (yes/no) was a stratification variable in an analysis of occurrence of acne relative to SEA tour. Time reference to SEA (pre- and post-SEA/post-SEA) was a stratification variable in the analysis of duration of acne and location of acne. The covariates age, race, and presence of pre-SEA acne were used in adjusted statistical analyses of all physical examination variables in the dermatologic evaluation. Age was used in its continuous form for modeling purposes for all dependent variables except comedones, where age was trichotomized. Age was also trichotomized for presentation purposes for dependent variable-covariate associations and interaction summaries.

### **Relation to Baseline and 1985 Followup Studies**

The same variables analyzed in the 1985 followup were analyzed in the 1987 followup. Except for depigmentation, which was a refinement in the analysis of the 1985 followup, the same variables were analyzed in the Baseline study.

The longitudinal analysis for the dermatologic evaluation was based on the dermatology index. For this analysis, the dermatology index was dichotomized as no abnormalities and at least one abnormality.

### **Statistical Methods**

Table 14-1 summarizes the statistical analyses that were performed for the dermatologic evaluation. The first part of this table describes the dependent variables analyzed and identifies the candidate covariates and the statistical methods used. The basic statistical analysis methods are described in Chapter 7. The second part of this table provides a further description of candidate covariates. Abbreviations are used extensively in the body of the table and are defined in footnotes.

Although no participants were excluded for medical reasons in the dermatologic assessment as stated above, some dependent variable and covariate data were missing. The number of participants with missing data is provided in Table 14-2 by group and variable.

TABLE 14-1.

## Statistical Analysis for the Dermatologic Evaluation

## Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Occurrence of Acne (Lifetime)	Q-SR	D	Yes No	--	UC:FT
Occurrence of Acne (Relative to SEA Tour)	Q-SR/ MIL	D	Pre-SEA Pre- and Post-SEA Post-SEA None	SEAACNE	UC:FT
Duration of Acne (years)	Q-SR	C	--	TIMESEA	UC:TT
Location of Acne	Q-SR	D	Temples Eyes Ears Other Sites	TIMESEA	UC:CS
Comedones	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Acneiform Lesions	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Acneiform Scars	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Depigmentation	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 14-1. (continued)

## Statistical Analysis for the Dermatologic Evaluation

## Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Inclusion Cysts	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Hyperpigmentation	PE	D	Yes No	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Other Abnormalities	PE	D	Normal: 0 Abnormal: $\geq 1$	AGE RACE OCC SEAACNE	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Dermatology Index	PE	D	0 1 2 3 4  Normal: 0 Abnormal: $\geq 1$	AGE RACE OCC SEAACNE  AGE RACE OCC SEAACNE	UC:FT AC:LL CA:CS  UE:CS,FT AE:LR L:OR

**TABLE 14-1. (continued)**  
**Statistical Analysis for the Dermatologic Evaluation**

<b>Covariates</b>			
Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born >1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Nonblack Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Time Reference of Acne Relative to SEA (TIMESEA)	Q-SR/ MIL	D	Pre- and Post-SEA Post-SEA
Presence of Pre-SEA Acne (SEAACNE)	Q-SR/ MIL	D	Yes No

**Abbreviations:**

**Data Source:** MIL--Air Force military records  
PE--1987 SCRF physical examination  
Q-SR--1987 NORC questionnaire (self-reported)

**Data Form:** C--Continuous analysis only  
D--Discrete analysis only  
D/C--Appropriate form for analysis (either discrete or continuous)

**Statistical Analyses:** UC--Unadjusted core analyses  
AC--Adjusted core analyses  
CA--Dependent variable-covariate associations  
UE--Unadjusted exposure index analyses  
AE--Adjusted exposure index analyses  
L--Longitudinal analyses

**Statistical Methods:** CS--Chi-square contingency table test  
FT--Fisher's exact test  
LL--Log-linear models analysis  
LR--Logistic regression analysis  
OR--Chi-square test on the odds ratio  
TT--Two-sample t-test

TABLE 14-2.

Number of Participants With Missing Data for  
Dermatology Evaluation by Group

Variable	Analysis Use	Group		Total
		Ranch Hand	Comparison	
Occurrence/Time Reference of Acne Relative to SEA	DEP/ COV	11	13	24
Presence of Pre-SEA Acne	COV	8	10	18

Abbreviations: COV--Covariate (missing data)  
DEP--Dependent variable (missing data)

**Note:** Six participants (three Ranch Hand and three Comparison) had acne before the start of their first SEA tour. These participants were not able to be classified distinctly as pre-SEA or pre- and post-SEA, however, which explains the difference in the number of missing participants for the two variables given above.

## RESULTS

### Ranch Hand and Comparison Group Contrast

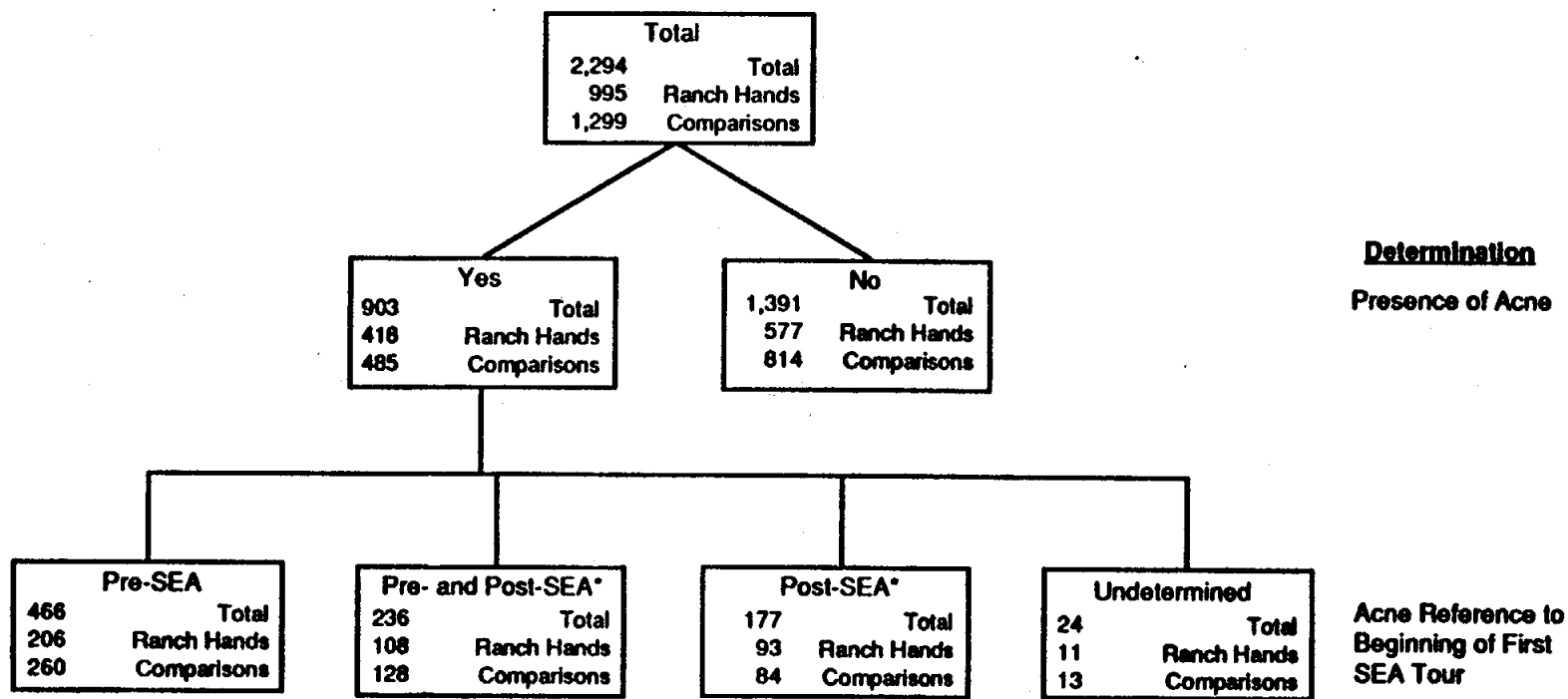
#### Questionnaire Variables

The occurrence of acne by time for the 2,294 participants in the 1987 followup is presented in Figure 14-1. The results of the analyses of the reported historical occurrence and duration of acne by group are provided in Table 14-3.

#### Occurrence of Acne

##### Lifetime

Of the 2,294 participants in the 1987 followup, 903 participants reported having experienced at least one occurrence of acne in their lifetime, and



**Yes to Acne** – Reported acne on Baseline and/or 1985 followup study and/or 1987 followup study.

**No to Acne** – Never had acne.

**Pre-SEA Acne** – Participants with acne who had all occurrences of acne before the start of first SEA tour (as determined from military records).

**Pre- and Post-SEA Acne** – Participants with acne who had multiple occurrences, both before and after the start of first SEA tour, or a case of acne that began before the start of first SEA tour and that ended after starting SEA tour.

**Post-SEA Acne** – Participants with acne who had all occurrences of acne after the start of first SEA tour.

**Undetermined** – Time reference not determinable from date information available.

\*: Analysis of duration and location of acne performed for these participants.

**Figure 14-1.  
Occurrence of Acne by Time for 1987 Followup Participants**

TABLE 14-3.

**Analysis of Reported Historical Occurrence  
and Duration of Acne by Group**

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Occurrence of Acne (Lifetime)	n	995	1,299		
	Number/%				
	Yes	418 42.0%	485 37.3%	1.22 (1.03,1.44)	0.026
	No	577 58.0%	814 62.7%		
Occurrence of Acne (Relative to SEA Tour)	n <sup>a</sup>	876	1,158		
	Number/%				
	Post-SEA vs.	93 10.6%	84 7.3%	1.52 (1.12,2.07)	0.010
	Pre-SEA/None	783 89.4%	1,074 92.7%		
	n	984	1,286		
Number/%					
	Post-SEA/Pre and Post-SEA vs.	201 20.4%	212 16.5%	1.30 (1.05,1.61)	0.019
	Pre-SEA/None	783 79.6%	1,074 83.5%		
	n <sup>b</sup>	670	898		
	Number/%				
	Post-SEA vs.	93 13.9%	84 9.4%	1.56 (1.14,2.14)	0.007
	None	577 86.1%	814 90.6%		

TABLE 14-3. (continued)

Analysis of Reported Historical Occurrence  
and Duration of Acne by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Duration of Acne	n <sup>c</sup>	314	388		
	Number/%				
	Pre- and Post- SEA vs.	108 34.4%	128 33.0%	1.07 (0.78,1.46)	0.754
	Pre-SEA	206 65.6%	260 67.0%		
	n <sup>d</sup>	92	2		
	Mean <sup>d</sup>	3.85	3.39	--	0.451
	95% C.I. <sup>d</sup>	(3.04,4.75)	(2.59,4.29)		
	n <sup>e</sup>	199	209		
	Mean <sup>e</sup>	9.17	9.69	--	0.611
	95% C.I. <sup>e</sup>	(7.82,10.64)	(8.33,11.17)		

<sup>a</sup>Participants with pre- and post-SEA acne excluded.

<sup>b</sup>Participants with no history of acne before the start of their first SEA tour.

<sup>c</sup>Participants with a prior occurrence of acne before the start of their first SEA tour.

<sup>d</sup>Transformed from square root scale; analysis based on participants with acne in the post-SEA category only.

<sup>e</sup>Transformed from square root scale; analysis based on participants with acne in the post-SEA category combined with participants in the pre- and post-SEA category.

1,391 participants said that they had never had acne. The analysis of self-reported lifetime occurrence of acne showed that significantly more Ranch Hands than Comparisons reported having had at least one occurrence of acne (42.0% vs. 37.3%,  $p=0.026$ ). The estimated relative risk was 1.22 (95% C.I.: [1.03,1.44]). Since the definition of lifetime includes periods of time before and after the SEA tour, this result alone does not indicate a herbicide effect. This analysis is further refined below for more direct applicability to this study; in particular, analyses relating to acne after the start of the first SEA tour were conducted.

#### Relative to SEA Tour

Participants with acne were further classified relative to their SEA tour(s) as determined by military records. Of the 903 participants with acne, 466 participants had all occurrences of acne prior to the start of their first SEA tour (pre-SEA), 236 participants had acne before and after the start of their first SEA tour (pre- and post-SEA), 177 participants reported having acne only after the start of their first SEA tour (post-SEA), and 24 participants could not be classified distinctly into one of these three categories due to incomplete information on dates of occurrence. These category names are used to assist the reader in identifying the contrasts in subsequent analyses.

To assess whether the occurrence of acne after the start of the first SEA tour was different between the two groups, analyses were conducted that contrasted participants with acne after the start of the first SEA tour with those who did not have acne after the start of the first SEA tour. Since it is difficult to determine whether the occurrence of acne could be related to dioxin exposure for the participants who had acne both before and after the start of their first SEA tour, the analysis was performed with and without the participants in the pre- and post-SEA category. The analysis of the occurrence of acne after the start of the first SEA tour was also performed after stratifying by occurrence of acne before the start of the first SEA tour. This analysis was done to determine if occurrence of acne before the start of the first SEA tour had any effect on occurrence of acne after the start of the first SEA tour. The three analyses that were conducted are listed below:

- Participants who had acne after the start of their first SEA tour, excluding those who had acne both before and after the start of their first SEA tour, versus participants who did not have acne after the start of their first SEA tour (post-SEA category vs. no acne and pre-SEA categories)
- Participants who only had acne after the start of their first SEA tour combined with those who had acne both before and after the start of their first SEA tour versus participants who did not have acne after the start of their first SEA tour (post-SEA and pre- and post-SEA categories vs. no acne and pre-SEA categories)

- Participants who had acne after the start of their first SEA tour versus participants who did not have acne after the start of their first SEA tour, stratified by occurrence of acne prior to their first SEA tour
  - Participants without acne prior to their first SEA tour: post-SEA category versus no acne category
  - Participants with acne prior to their first SEA tour: pre- and post-SEA category versus pre-SEA category

The results of these analyses are presented below.

In the first analysis, the 177 participants who only had acne after the start of their first SEA tour were contrasted with the 1,391 participants who never had acne combined with the 466 participants who only had acne before the start of their first SEA tour. The result of this analysis showed that the Ranch Hands had a significantly higher prevalence of acne (Est. RR: 1.52, 95% C.I.: [1.12, 2.07],  $p=0.010$ ). Of the Ranch Hands, 10.6 percent had an occurrence of acne, as opposed to 7.3 percent of the Comparisons.

When the 236 participants who had acne before and after the start of their SEA tour were included in the analysis, a significant difference was also detected (Est. RR: 1.30, 95% C.I.: [1.05, 1.61],  $p=0.019$ ). The Ranch Hands had a prevalence rate of 20.4 percent, as contrasted with a prevalence rate of 16.5 percent in the Comparisons.

In the analysis stratified by the occurrence of acne prior to the first SEA tour, a significant group difference was detected for those who did not have an occurrence of acne before their first SEA tour (Est. RR: 1.56, 95% C.I.: [1.14, 2.14],  $p=0.007$ ). Of the Ranch Hands with no history of acne before the start of the first SEA tour, 13.9 percent had an occurrence of acne after the start of the first SEA tour. Only 9.4 percent of the Comparisons had acne for the first time after the start of the first SEA tour. However, no significant difference was found between groups for participants with an occurrence of acne before the first SEA tour ( $p=0.754$ ).

#### Duration of Acne

Analysis of duration of acne was performed for participants in the post-SEA category and in the post-SEA and pre- and post-SEA categories combined. A square root transformation was applied to the duration data for analysis purposes. No significant differences between the Ranch Hands and the Comparisons were detected in the analysis of duration of acne ( $p=0.451$  for participants in the post-SEA acne category and  $p=0.611$  for participants in the post-SEA and pre- and post-SEA acne categories combined).

#### Location of Acne

The location of acne was analyzed for the participants in the post-SEA acne category and those in the post-SEA and pre- and post-SEA categories

combined. The spatial distributions of acne with primary emphasis on the temples, around the eyes, or on the ears are presented in Figures 14-2 and 14-3. The distributions provided in Figure 14-2 are limited to the participants in the post-SEA only category. Figure 14-3 shows the distribution of acne by location for the Ranch Hands and Comparisons in the post-SEA and pre- and post-SEA categories combined.

No differences in the spatial distributions for the two groups were detected when the analysis was limited to the post-SEA category ( $p=0.274$  with other sites included and  $p=0.339$  with other sites excluded).

Based on the combined post-SEA and pre- and post-SEA categories, no difference in the spatial distribution between the two groups was noted ( $p=0.442$ ). There was also no significant difference when the location of other sites was eliminated from the analysis ( $p=0.566$ ).

### Physical Examination Variables

Eight variables from the physical examination were analyzed in the dermatologic assessment. Table 14-4 provides the results of the unadjusted analyses. The results of the adjusted analyses are presented in Table 14-5. Table K-1 of Appendix K contains the results of the dependent variable-covariate associations.

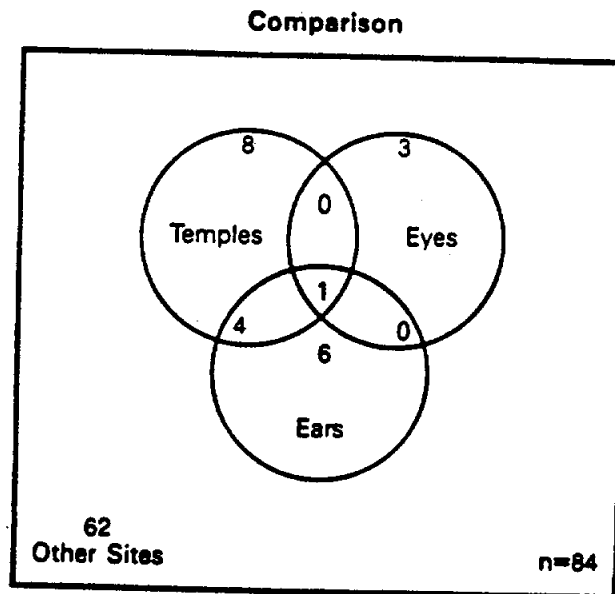
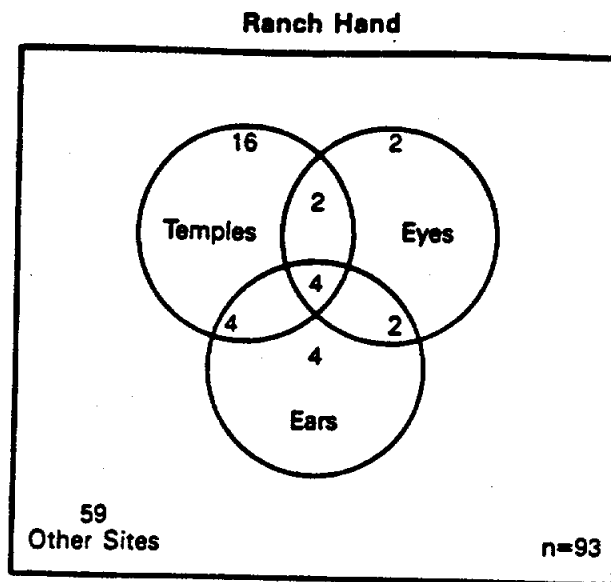
There were no cases of chloracne diagnosed at the 1987 followup.

### Comedones

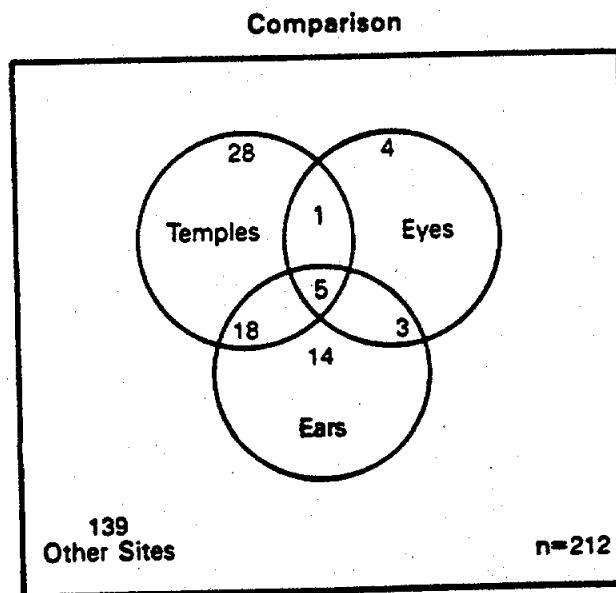
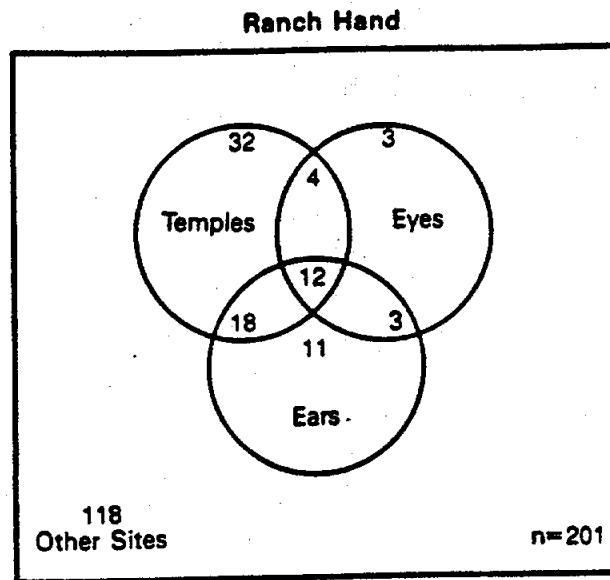
There was no significant difference between the percentage of Ranch Hands and Comparisons with comedones based on the unadjusted analysis ( $p=0.436$ ).

As shown in Table K-1 of Appendix K, the covariate tests revealed significant associations for age and occupation ( $p<0.001$  for both). The percentage of participants with comedones was highest among those born between 1923 and 1941 (25.4%), followed by those born in or before 1922 (22.6%) and those born in or after 1942 (18.1%). For occupation, 17.0 percent of the officers, 33.2 percent of the enlisted flyers, and 22.6 percent of the enlisted groundcrew had comedones.

In the adjusted analysis of comedones, there was a significant group-by-race interaction ( $p=0.049$ ). Occupation and age-by-presence of pre-SEA acne were also significant terms in the model ( $p<0.001$  and  $p=0.027$ , respectively). As shown in Table K-2 of Appendix K, the Black Ranch Hands had a marginally higher prevalence rate than the Black Comparisons (Adj. RR: 2.33, 95% C.I.: [0.90, 6.08],  $p=0.083$ ). No significant difference was detected between the nonblack Ranch Hands and Comparisons ( $p=0.213$ ). Without the group-by-race interaction in the model, there was no significant difference between the two groups ( $p=0.396$ ).



**Figure 14-2.**  
**Location of Post-SEA**  
**Acne by Group**



**Figure 14-3.**  
**Location of Post-SEA and Pre-**  
**and Post-SEA Acne by Group**

TABLE 14-4.

## Unadjusted Analysis for Dermatology Variables by Group

Variable	Statistic	Group		Contrast	Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison			
Comedones	n	995	1,299			
	Number/%					
	Yes	213 21.4%	297 22.9%		0.92 (0.75,1.12)	0.436
	No	782 78.6%	1,002 77.1%			
Acneiform Lesions	n	995	1,299			
	Number/%					
	Yes	101 10.2%	145 11.2%		0.90 (0.69,1.18)	0.480
	No	894 89.8%	1,154 88.8%			
Acneiform Scars	n	995	1,299			
	Number/%					
	Yes	118 11.9%	139 10.7%		1.12 (0.87,1.46)	0.420
	No	877 88.1%	1,160 89.3%			
Depigmentation	n	995	1,299			
	Number/%					
	Yes	66 6.6%	83 6.4%		1.04 (0.75,1.45)	0.878
	No	929 93.4%	1,216 93.6%			

TABLE 14-4. (continued)

## Unadjusted Analysis for Dermatology Variables by Group

Variable	Statistic	Group		Contrast	Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison			
Inclusion Cysts	n	995	1,299			
	Number/%					
	Yes	105 10.6%	136 10.5%		1.01 (0.77,1.32)	0.999
	No	890 89.4%	1,163 89.5%			
Hyperpigmentation	n	995	1,299			
	Number/%					
	Yes	146 14.7%	218 16.8%		0.85 (0.68,1.07)	0.189
	No	849 85.3%	1,081 83.2%			
Other Abnormalities	n	995	1,299			
	Number/%					
	Abnormal	759 76.3%	969 74.6%		1.10 (0.90,1.33)	0.380
	Normal	236 23.7%	330 25.4%			
Dermatology Index	n	995	1,299			
	Number/%					
	0	609 61.2%	800 61.6%	Overall		0.636
	1	273 27.4%	334 25.7%	1 vs. 0	1.07 (0.89,1.30)	0.496
	2	84 8.4%	121 9.3%	2 vs. 0	0.91 (0.68,1.23)	0.596
	3	20 2.0%	35 2.7%	3 vs. 0	0.75 (0.43,1.31)	0.386
	4	9 0.9%	9 0.7%	4 vs. 0	1.31 (0.52,3.33)	0.730

TABLE 14-5.

## Adjusted Analysis for Dermatology Variables by Group

Variable	Statistic	Group		Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison				
Comedones	n	987	1,289		0.92 (0.75,1.12)**	0.396**	GRP*RACE (p=0.049) OCC (p<0.001) AGE*SEAAONE (p=0.027)
Acneiform Lesions	n	987	1,289		0.90 (0.68,1.18)	0.426	AGE (p<0.001) SEAAONE (p<0.001)
Acneiform Scars	n	987	1,289		1.10 (0.84,1.43)	0.510	AGE (p=0.010) SEAAONE (p<0.001)
Depigmentation	n	995	1,299		1.04 (0.74,1.45)	0.838	AGE (p=0.010)
Inclusion Cysts	n	987	1,289		1.00 (0.76,1.31)	0.965	AGE (p=0.032) RACE*SEAAONE (p=0.035)
Hyperpigmentation	n	987	1,289		0.86 (0.68,1.09)	0.206	RACE (p<0.001) OCC (p<0.001) SEAAONE (p=0.006)

TABLE 14-5. (continued)

## Adjusted Analysis for Dermatology Variables by Group

Variable	Statistic	Group		Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison				
Other Abnormalities	n	995	1,299		1.08 (0.89,1.32)	0.445	RACE (p<0.001) AGE (p<0.001)
Dermatology Index	n	987	1,289	Overall		0.679	OCC (p<0.001)
				1 vs. 0	1.06 (0.88,1.28)	0.532	AGE*SEAAONE (p=0.029)
				2 vs. 0	0.91 (0.67,1.23)	0.524	
				3 vs. 0	0.76 (0.44,1.32)	0.332	
				4 vs. 0	1.28 (0.55,3.01)	0.569	

GRP: Group (Ranch Hand, Comparison).

\*\*Group-by-covariate interaction (0.01<p<0.05)—adjusted relative risk, confidence interval, and p-value presented derived from a model fitted after deletion of this interaction.

### Acneiform Lesions

In the unadjusted analysis of acneiform lesions, no significant difference was detected between the two groups ( $p=0.480$ ).

Using pooled group data, the covariate associations with acneiform lesions showed that age, occupation, and presence of pre-SEA acne were significant ( $p<0.001$ ,  $p=0.001$ , and  $p<0.001$ , respectively). The presence of acneiform lesions was found to be decreasing with age (15.1% for those born in or after 1942, 7.8% for those born between 1923 and 1941, and 4.8% for those born in or before 1922). The highest percentage of participants with acneiform lesions was among the enlisted groundcrew (13.1%), followed by the enlisted flyers (10.7%) and the officers (7.9%). The percentage of participants with acneiform lesions was higher for those with pre-SEA acne than those who did not have pre-SEA acne (15.3% vs. 8.7%).

Based on the adjusted analysis of acneiform lesions, there was no significant difference between the Ranch Hands and the Comparisons ( $p=0.426$ ). Age and presence of pre-SEA acne were significant covariates in the adjusted model ( $p<0.001$  for both).

### Acneiform Scars

The results of unadjusted analyses of acneiform scars did not reveal a significant difference between the Ranch Hands and the Comparisons ( $p=0.420$ ).

The significant covariate relationships with acneiform scars were age and presence of pre-SEA acne ( $p=0.005$  and  $p<0.001$ , respectively). The association between acneiform scars and occupation was marginally significant ( $p=0.051$ ). The percentage of participants with acneiform scars decreased with age (13.6% for those born in or after 1942, 9.7% for those born between 1923 and 1941, and 6.0% for those born in or before 1922). For occupation, 9.2 percent of the officers had acneiform scars, as compared to 12.5 percent of the enlisted flyers and 12.4 percent of the enlisted groundcrew. The participants with pre-SEA acne had a higher prevalence rate than those without pre-SEA acne (22.5% vs. 6.2%).

In the adjusted analysis of acneiform scars, there was no significant difference between the two groups ( $p=0.510$ ). The significant covariates in the model were age and presence of pre-SEA acne ( $p=0.010$  and  $p<0.001$ , respectively).

### Depigmentation

No significant difference between the two groups was identified based on the unadjusted analysis of depigmentation ( $p=0.878$ ).

Only the depigmentation-age association was found to be significant ( $p=0.034$ ). The prevalence rate increased with age. Of the participants born in or after 1942, 5.3 percent had depigmentation, as compared to 7.0 percent of those born between 1923 and 1941 and 11.9 percent of those born in or before 1922.

The results of the adjusted analysis of depigmentation did not reveal a significant group difference ( $p=0.838$ ). Age was a significant covariate in the model ( $p=0.010$ ).

### Inclusion Cysts

The unadjusted analysis of inclusion cysts did not reveal a significant difference between the Ranch Hands and the Comparisons ( $p=0.999$ ).

The covariate tests for inclusion cysts showed that the relationship with race was significant ( $p=0.035$ ), and the associations with age, occupation, and presence of pre-SEA acne were borderline significant ( $p=0.096$ ,  $p=0.063$ , and  $p=0.092$ , respectively). For age, the highest percentage of participants with inclusion cysts was among those born between 1923 and 1941 (11.7%), followed by those born in or before 1922 (10.7%) and those born in or after 1942 (8.9%). The prevalence rate was higher for nonblacks than Blacks (10.8% vs. 5.1%). For occupation, 10.1 percent of the officers, 13.8 percent of the enlisted flyers, and 9.6 percent of the enlisted groundcrew had inclusion cysts. A higher percentage of the participants with pre-SEA acne had inclusion cysts than those without pre-SEA acne (12.3% vs. 9.8%).

Based on the adjusted analysis of inclusion cysts, there was no significant difference between the two groups ( $p=0.965$ ). Age and race-by-presence of pre-SEA acne were significant terms in the model ( $p=0.032$  and  $p=0.035$ , respectively).

### Hyperpigmentation

Based on the analysis of hyperpigmentation without adjustments for covariates, no difference was found between the two groups ( $p=0.189$ ).

Significant relationships were found between hyperpigmentation and race, occupation, and presence of pre-SEA acne ( $p<0.001$ ,  $p<0.001$ , and  $p=0.003$ , respectively). The prevalence rate for Blacks was higher than for nonblacks (35.8% vs. 14.6%). For occupation, the prevalence rate was highest for the enlisted groundcrew (19.8%), followed by the enlisted flyers (19.6%) and the officers (9.6%). A higher percentage of the participants without pre-SEA acne had hyperpigmentation than those with pre-SEA acne (17.3% vs. 12.4%).

The results of the adjusted analysis of hyperpigmentation did not reveal a significant difference between the two groups ( $p=0.206$ ). The significant terms in the model were race, occupation, and presence of pre-SEA acne ( $p<0.001$ ,  $p<0.001$ , and  $p=0.006$ , respectively).

### Other Abnormalities

After combining all other dermatologic abnormalities to create a composite variable, there was no significant difference between the Ranch Hands and the Comparisons based on the unadjusted analysis ( $p=0.380$ ).

The results of the covariate tests did not detect a significant association for presence of pre-SEA acne; however, significant relationships were found for age, race, and occupation ( $p < 0.001$  for all). The prevalence rate of other abnormalities increased with age (65.2% for those born in or after 1942, 82.0% for those born between 1923 and 1941, and 90.5% for those born in or before 1922). A higher percentage of nonblacks than Blacks had a dermatologic abnormality, other than the six conditions analyzed previously (76.8% vs. 51.8%). The highest percentage of other abnormalities was in the officers (79.2%), followed by the enlisted flyers (78.3%) and the enlisted groundcrew (71.0%).

No significant difference between the Ranch Hands and the Comparisons was identified in the adjusted analysis of other abnormalities ( $p = 0.445$ ). Age and race were significant covariates in the model ( $p < 0.001$  for both).

### Dermatology Index

There was no significant difference between the two groups based on the overall unadjusted analysis of the dermatology index ( $p = 0.636$ ), which was based on the number of abnormalities present for the following conditions: comedones, acneiform lesions, acneiform scars, and inclusion cysts. The results of the four individual contrasts of one, two, three, and four abnormalities versus zero abnormalities also did not detect any significant differences between the Ranch Hands and the Comparisons ( $p = 0.496$  for 1 vs. 0,  $p = 0.596$  for 2 vs. 0,  $p = 0.386$  for 3 vs. 0, and  $p = 0.730$  for 4 vs. 0).

The covariate tests for the dermatology index revealed significant associations with occupation and presence of pre-SEA acne ( $p < 0.001$  for both). These results are presented in tabular form in Table K-1 of Appendix K.

Overall, the officers had the highest percentage of participants with no abnormalities on the dermatology index (67.4% with zero abnormalities), followed by the enlisted groundcrew (59.8% with zero abnormalities), and the enlisted flyers (52.2% with zero abnormalities). The enlisted flyers had the highest percentage of abnormalities in the one and two abnormality classes of the index, and the officers had the lowest percentages (one abnormality: 30.0% for enlisted flyers, 27.0% for enlisted groundcrew, and 24.3% for officers; two abnormalities: 14.1% for enlisted flyers, 9.5% for enlisted groundcrew, and 6.1% for officers). For three abnormalities, the percentages were 3.2 for enlisted groundcrew, 2.6 for enlisted flyers, and 1.4 for officers. For four abnormalities, the highest percentage was among the enlisted flyers (1.0%), followed by the officers (0.9%) and the enlisted groundcrew (0.6%).

A greater percentage of participants with pre-SEA acne than those without pre-SEA acne had abnormalities based on the dermatology index. Only 53.7 percent of those with pre-SEA acne had no abnormalities, as compared to 64.9 percent of those without pre-SEA acne. Of those with pre-SEA acne, 27.0 percent had one abnormality, 13.7 percent had two abnormalities, 4.4 percent had three abnormalities, and 1.3 percent had four abnormalities. For the participants without pre-SEA acne, 26.2 percent had one abnormality, 6.8 percent had two abnormalities, 1.5 percent had three abnormalities, and 0.6 percent had four abnormalities.

No significant difference was found in the adjusted analysis of the dermatology index ( $p=0.679$ ). This finding was supported by the results of the four individual contrasts ( $p=0.532$  for 1 vs. 0,  $p=0.524$  for 2 vs. 0,  $p=0.332$  for 3 vs. 0, and  $p=0.569$  for 4 vs. 0). Occupation and age-by-presence of pre-SEA acne were significant terms in the adjusted model ( $p<0.001$  and  $p=0.029$ , respectively).

### Biopsy Results

Dermatologists were instructed to request skin biopsies of any lesions suspected of being malignant. The histologic classifications of the 39 skin biopsies performed in the 1987 followup are summarized in Table 14-6. Of these biopsies, 27 were classified as basal cell carcinoma. There was no significant difference in the number of men in each group who had biopsies (Est. RR: 1.03, 95% C.I.: [0.52, 2.04]  $p=0.930$ ) or in the number of biopsied participants who had a basal cell carcinoma (Est. RR: 2.0, 95% C.I.: [0.46, 8.63]  $p=0.350$ ). A more complete discussion of the post-SEA lifetime occurrence of basal cell carcinoma can be found in Chapter 10, Malignancy.

### Exposure Index Analysis

Unadjusted and adjusted exposure index analyses were conducted on the physical examination variables of the dermatologic assessment; the results of these analyses are presented in Tables 14-7 and 14-8, respectively. A summary of the exposure index-by-covariate interactions is provided in Table 14-9. The detailed stratified results for the exposure index-by-covariate interactions are listed in Table K-3 of Appendix K.

The final interpretation of the exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. This report is expected in 1991.

### Physical Examination Variables

#### Comedones

No significant differences among the exposure categories were detected in the unadjusted analyses. These findings were supported by the results of the adjusted analyses for the enlisted flyer and enlisted groundcrew cohorts.

In the adjusted analysis of the officer cohort, there was a significant exposure index-by-presence of pre-SEA acne interaction ( $p=0.014$ ). Of the officers with pre-SEA acne, 21.4 percent in the low exposure category had comedones as compared to 14.6 percent in the medium exposure category and 4.7 percent in the high exposure category. The high versus low exposure contrast for the pre-SEA acne stratum was significant ( $p=0.046$ ), although the result was not supportive of an increasing dose-response relationship. For the officers without pre-SEA acne, the percentages with comedones were 9.9, 13.3, and 21.0 for the low, medium, and high exposure categories, respectively. The high versus low exposure contrast for those without pre-SEA acne was marginally significant ( $p=0.080$ ). Without this exposure index-by-presence of pre-SEA interaction in the model, no significant differences were found among the exposure level categories.

TABLE 14-6.

## Histologic Classification of Skin Biopsies at the 1987 Followup

Histologic Type	Group	
	Ranch Hand	Comparison
Basal Cell Carcinoma	15 <sup>a</sup>	12 <sup>b</sup>
Melanoma	1	0
Suspected Squamous Cell Carcinoma	0	1 <sup>c</sup>
Keratosis, Actinic	1	2
Keratosis, Seborrheic	1	1
Papilloma, Benign	0	1
Nevus, Compound	1	2
Cyst, Epidermal	0	1
	19	20

<sup>a</sup>Two individuals had basal cell carcinomas at two separate sites, and one individual had basal cell carcinomas at three separate sites.

<sup>b</sup>One individual had basal cell carcinomas at two separate sites.

<sup>c</sup>Squamous cell carcinoma could not be equivocally excluded on submarginal tissue.

TABLE 14-7.

## Unadjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Comedones	Officer	n	130		124		125		Overall		0.798
		Number/%									
		Yes	16	12.3%	17	13.7%	19	15.2%	M vs. L	1.13 (0.54,2.35)	0.884
	Enlisted Flyer	No	114	87.7%	107	86.3%	106	84.8%	H vs. L	1.28 (0.62,2.61)	0.624
		n	55		63		53		Overall		0.352
		Number/%									
	Enlisted Groundcrew	Yes	18	32.7%	17	27.0%	21	39.6%	M vs. L	0.76 (0.34,1.68)	0.632
		No	37	67.3%	46	73.0%	32	60.4%	H vs. L	1.35 (0.61,2.97)	0.586
		n	147		158		140		Overall		0.860
		Number/%									
		Yes	37	25.2%	36	22.8%	32	22.9%	M vs. L	0.88 (0.52,1.49)	0.724
		No	110	74.8%	122	77.2%	108	77.1%	H vs. L	0.88 (0.51,1.52)	0.750
Acneiform Lesions	Officer	n	130		124		125		Overall		0.378
		Number/%									
		Yes	10	7.7%	7	5.6%	13	10.4%	M vs. L	0.72 (0.26,1.95)	0.690
	Enlisted Flyer	No	120	92.3%	117	94.4%	112	89.6%	H vs. L	1.39 (0.59,3.30)	0.592
		n	55		63		53		Overall		0.483
		Number/%									
	Enlisted Groundcrew	Yes	3	5.5%	7	11.1%	6	11.3%	M vs. L	2.17 (0.53,8.82)	0.446
		No	52	94.5%	56	88.9%	47	88.7%	H vs. L	2.21 (0.52,9.35)	0.452
		n	147		158		140		Overall		0.571
		Number/%									
		Yes	19	12.9%	22	13.9%	14	10.0%	M vs. L	1.09 (0.56,2.11)	0.932
		No	128	87.1%	136	86.1%	126	90.0%	H vs. L	0.75 (0.36,1.56)	0.556

TABLE 14-7. (continued)

## Unadjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Acneiform Scars	Officer	n	130		124		125		Overall		0.600	
		Number/%										
		Yes	10	7.7%	14	11.3%	11	8.8%	M vs. L	1.53 (0.65,3.58)	0.444	
		No	120	92.3%	110	88.7%	114	91.2%	H vs. L	1.16 (0.47,2.83)	0.924	
		Enlisted Flyer	n	55		63		53		Overall		0.333
			Number/%									
	Yes		7	12.7%	5	7.9%	9	17.0%	M vs. L	0.59 (0.18,1.98)	0.578	
		No	48	87.3%	58	92.1%	44	83.0%	H vs. L	1.40 (0.48,4.09)	0.726	
		Enlisted Groundcrew	n	147		158		140		Overall		0.879
Number/%												
Depigmentation			Yes	19	12.9%	22	13.9%	21	15.0%	M vs. L	1.09 (0.56,2.11)	0.932
		No	128	87.1%	136	86.1%	119	85.0%	H vs. L	1.19 (0.61,2.32)	0.736	
		n	130		124		125		Overall		0.610	
		Number/%										
		Yes	6	4.6%	6	4.8%	9	7.2%	M vs. L	1.05 (0.33,3.35)	0.999	
		No	124	95.4%	118	95.2%	116	92.8%	H vs. L	1.60 (0.55,4.65)	0.542	
	Enlisted Flyer	n	55		63		53		Overall		0.253	
		Number/%										
		Yes	8	14.5%	5	7.9%	3	5.7%	M vs. L	0.51 (0.16,1.65)	0.396	
		No	47	85.5%	58	92.1%	50	94.3%	H vs. L	0.35 (0.09,1.41)	0.226	
		Enlisted Groundcrew	n	147		158		140		Overall		0.074
			Number/%									
	Yes		4	2.7%	13	8.2%	12	8.6%	M vs. L	3.21 (1.02,10.06)	0.061	
		No	143	97.3%	145	91.8%	128	91.4%	H vs. L	3.35 (1.05,10.65)	0.055	

TABLE 14-7. (continued)

## Unadjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value	
			Low		Medium		High					
Inclusion Cysts	Officer	n	130		124		125		Overall		0.587	
		Number/%										
		Yes	13	10.0%	8	6.5%	11	8.8%	M vs. L	0.62 (0.25,1.55)	0.426	
		No	117	90.0%	116	93.5%	114	91.2%	H vs. L	0.87 (0.37,2.02)	0.999	
		Enlisted Flyer	n	55		63		53		Overall		0.774
			Number/%									
	Yes		8	14.5%	10	15.9%	6	11.3%	M vs. L	1.11 (0.40,3.04)	0.999	
		No	47	85.5%	53	84.1%	47	88.7%	H vs. L	0.75 (0.24,2.33)	0.834	
		Enlisted Groundcrew	n	147		158		140		Overall		0.650
Number/%												
Yes	16		10.9%	15	9.5%	18	12.9%	M vs. L	0.86 (0.41,1.81)	0.832		
Hyperpigmentation	Officer	No	131	89.1%	143	90.5%	122	87.1%	H vs. L	1.21 (0.59,2.48)	0.738	
		n	130		124		125		Overall		0.359	
		Number/%										
		Yes	10	7.7%	13	10.5%	7	5.6%	M vs. L	1.41 (0.59,3.33)	0.578	
		No	120	92.3%	111	89.5%	118	94.4%	H vs. L	0.71 (0.26,1.93)	0.678	
		Enlisted Flyer	n	55		63		53		Overall		0.907
	Number/%											
	Yes		11	20.0%	11	17.5%	9	17.0%	M vs. L	0.85 (0.34,2.14)	0.904	
		No	44	80.0%	52	82.5%	44	83.0%	H vs. L	0.82 (0.31,2.17)	0.878	
		Enlisted Groundcrew	n	147		158		140		Overall		0.341
			Number/%									
	Yes		25	17.0%	36	22.8%	24	17.1%	M vs. L	1.44 (0.82,2.54)	0.264	
	No	122	83.0%	122	77.2%	116	82.9%	H vs. L	1.01 (0.55,1.87)	0.999		

TABLE 14-7. (continued)

## Unadjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index						Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
			Low		Medium		High				
Other Abnormalities	Officer	n	130		124		125		Overall		0.042
		Number/% Abnormal	101	77.7%	110	88.7%	98	78.4%	M vs. L	2.26 (1.13,4.51)	0.029
		Normal	29	22.3%	14	11.3%	27	21.6%	H vs. L	1.04 (0.58,1.89)	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.036
		Number/% Abnormal	47	85.5%	44	69.8%	46	86.8%	M vs. L	0.39 (0.16,0.99)	0.071
		Normal	8	14.5%	19	30.2%	7	13.2%	H vs. L	1.12 (0.38,3.34)	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.272
		Number/% Abnormal	103	70.1%	105	66.5%	105	75.0%	M vs. L	0.85 (0.52,1.37)	0.580
		Normal	44	29.9%	53	33.5%	35	25.0%	H vs. L	1.28 (0.76,2.16)	0.422
Dermatology Index	Officer	n	130		124		125		Overall		0.625
		Number/% Abnormal	38	29.2%	37	29.8%	43	34.4%	M vs. L	1.03 (0.60,1.77)	0.999
		Normal	92	70.8%	87	70.2%	82	65.6%	H vs. L	1.27 (0.75,2.15)	0.452
	Enlisted Flyer	n	55		63		53		Overall		0.434
		Number/% Abnormal	24	43.6%	28	44.4%	29	54.7%	M vs. L	1.03 (0.50,2.14)	0.999
		Normal	31	56.4%	35	55.6%	24	45.3%	H vs. L	1.56 (0.73,3.34)	0.338
	Enlisted Groundcrew	n	147		158		140		Overall		0.481
		Number/% Abnormal	65	44.2%	69	43.7%	53	37.9%	M vs. L	0.98 (0.62,1.54)	0.999
		Normal	82	55.8%	89	56.3%	87	62.1%	H vs. L	0.77 (0.48,1.23)	0.330

TABLE 14-8.

## Adjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Comedones	Officer	n	129	123	124	Overall		0.908**
						M vs. L	1.14 (0.53,2.43)**	0.742**
						H vs. L	1.18 (0.56,2.48)**	0.673**
	Enlisted Flyer	n	55	63	52	Overall		0.407
						M vs. L	0.91 (0.40,2.05)	0.815
						H vs. L	1.52 (0.68,3.41)	0.308
	Enlisted Groundcrew	n	146	157	138	Overall		0.623
						M vs. L	1.13 (0.65,1.96)	0.669
						H vs. L	0.85 (0.48,1.50)	0.574
Acneiform Lesions	Officer	n	129	123	124	Overall		0.180
						M vs. L	0.57 (0.19,1.71)	0.314
						H vs. L	1.45 (0.57,3.69)	0.437
	Enlisted Flyer	n	55	63	52	Overall		0.412
						M vs. L	2.16 (0.52,9.01)	0.290
						H vs. L	2.44 (0.57,10.49)	0.230
	Enlisted Groundcrew	n	146	157	138	Overall		****
						M vs. L	****	****
						H vs. L	****	****

TABLE 14-8. (continued)

## Adjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Acneiform Scars	Officer	n	129	123	124	Overall		0.874**
						M vs. L	1.16 (0.46,2.89)**	0.751**
						H vs. L	0.93 (0.36,2.39)**	0.874**
	Enlisted Flyer	n	55	63	52	Overall		0.273
						M vs. L	0.59 (0.17,2.09)	0.416
						H vs. L	1.58 (0.52,4.82)	0.421
	Enlisted Groundcrew	n	146	157	138	Overall		0.526**
						M vs. L	1.05 (0.53,2.11)**	0.882**
						H vs. L	1.46 (0.72,2.94)**	0.297**
Depigmentation	Officer	n	129	123	124	Overall		0.469
						M vs. L	0.69 (0.21,2.31)	0.547
						H vs. L	1.37 (0.46,4.07)	0.570
	Enlisted Flyer	n	55	63	52	Overall		0.264
						M vs. L	0.51 (0.15,1.68)	0.266
						H vs. L	0.35 (0.09,1.40)	0.138
	Enlisted Groundcrew	n	146	157	138	Overall		0.040**
						M vs. L	3.34 (1.05,10.59)**	0.040**
						H vs. L	3.54 (1.11,11.34)**	0.033**

TABLE 14-8. (continued)

## Adjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Inclusion Cysts	Officer	n	129	123	124	Overall		0.606
						M vs. L	0.62 (0.24,1.61)	0.331
						H vs. L	0.87 (0.37,2.05)	0.745
	Enlisted Flyer	n	55	63	52	Overall		0.687
						M vs. L	1.30 (0.46,3.64)	0.620
						H vs. L	0.80 (0.26,2.53)	0.709
Hyperpigmentation	Enlisted Groundcrew	n	146	157	138	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Officer	n	129	123	124	Overall		0.421
						M vs. L	1.12 (0.46,2.75)	0.801
						H vs. L	0.61 (0.22,1.68)	0.340
	Enlisted Flyer	n	55	63	52	Overall		0.852
						M vs. L	0.81 (0.31,2.08)	0.660
						H vs. L	0.76 (0.28,2.07)	0.597
	Enlisted Groundcrew	n	146	157	138	Overall		0.247
						M vs. L	1.53 (0.85,2.77)	0.157
						H vs. L	0.99 (0.52,1.86)	0.966

TABLE 14-8. (continued)

## Adjusted Exposure Index for Dermatology Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Other Abnormalities	Officer	n	129	123	124	Overall		0.040
						M vs. L	2.12 (1.00,4.47)	0.049
						H vs. L	0.89 (0.47,1.68)	0.714
	Enlisted Flyer	n	55	63	52	Overall		0.069
						M vs. L	0.42 (0.16,1.06)	0.067
						H vs. L	1.08 (0.36,3.26)	0.888
	Enlisted Groundcrew	n	146	157	138	Overall		0.512
						M vs. L	0.93 (0.56,1.53)	0.777
						H vs. L	1.26 (0.73,2.16)	0.405
Dermatology Index	Officer	n	129	123	124	Overall		0.568
						M vs. L	1.17 (0.66,2.07)	0.589
						H vs. L	0.87 (0.50,1.50)	0.619
	Enlisted Flyer	n	55	63	52	Overall		0.335
						M vs. L	0.83 (0.39,1.77)	0.634
						H vs. L	0.56 (0.26,1.23)	0.149
	Enlisted Groundcrew	n	146	157	138	Overall		0.383**
						M vs. L	0.96 (0.61,1.52)**	0.870**
						H vs. L	1.31 (0.81,2.12)**	0.263**

\*\*\*Exposure index-by-covariate interaction ( $p < 0.01$ )—relative risk, confidence interval, and p-value not presented.

\*\*Exposure index-by-covariate interaction ( $0.01 < p < 0.05$ )—relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

TABLE 14-9.

**Summary of Exposure Index-by-Covariate Interactions  
From Adjusted Analyses for Dermatology Variables\***

Variable	Occupation	Covariate	p-Value
Comedones	Officer	Presence of Pre-SEA Acne	0.014
Acneiform Lesions	Enlisted Groundcrew	Presence of Pre-SEA Acne	0.009
Acneiform Scars	Officer	Age	0.021
Acneiform Scars	Enlisted Groundcrew	Race	0.045
Depigmentation	Enlisted Groundcrew	Race	0.023
Inclusion Cysts	Enlisted Groundcrew	Presence of Pre-SEA Acne	0.005
Dermatology Index	Enlisted Groundcrew	Presence or Pre-SEA Acne	0.025

\*Refer to Table K-3 for a further investigation of these interactions.

#### Acneiform Lesions

For the officer and enlisted flyer cohorts, there were no significant differences among the exposure categories in either the unadjusted or adjusted analyses.

Based on the unadjusted analysis of the enlisted groundcrew cohort, there were no significant differences. In the adjusted analysis, there was a significant exposure index-by-presence of pre-SEA acne interaction ( $p=0.009$ ). After stratifying by presence of pre-SEA acne, the high versus low exposure contrast for those without pre-SEA acne was significant ( $p=0.049$ ) although the result was not suggestive of an increasing dose-response relationship. For the enlisted groundcrew without pre-SEA acne, the percentages with acneiform lesions were 13.4, 15.8, and 5.2 for the low, medium, and high exposure categories, respectively.

#### Acneiform Scars

The results of the unadjusted analyses did not reveal any significant differences among the exposure categories for the three occupational cohorts. These findings were supported by the adjusted results of the enlisted flyer cohort and the adjusted results of the officer and enlisted groundcrew cohorts without significant interactions in the models.

In the adjusted analysis of the officer cohort, there was a significant exposure index-by-age interaction ( $p=0.021$ ). After stratifying by age, the results showed that the medium versus low exposure contrast for those born between 1923 and 1941 was significant ( $p=0.030$ ). Of the officers born between 1923 and 1941, 3.8 percent in the low exposure category, 14.8 percent in the

medium exposure category, and 8.2 percent in the high exposure category had acneiform scars. The high versus low exposure contrast for this stratum was not significant.

In the enlisted groundcrew cohort, the exposure index-by-race interaction was significant ( $p=0.045$ ). After stratifying by race, no significant differences were detected.

### Depigmentation

There were no significant differences identified in either the unadjusted or adjusted analyses of the officer and enlisted flyer cohorts.

In the enlisted groundcrew cohort, the percentages with depigmentation were 2.7, 8.2, and 8.6 in the low, medium, and high exposure categories, respectively. In the unadjusted analysis, the overall, medium versus low, and high versus low contrasts were marginally significant ( $p=0.074$ ,  $p=0.061$ , and  $p=0.055$ , respectively). In the adjusted analysis of the enlisted groundcrew cohort, there was a significant exposure index-by-race interaction ( $p=0.023$ ). Although there were no significant results for Blacks, significant differences were detected for nonblacks. For the nonblacks, the highest percentage of abnormalities was in the medium exposure category (9.0%) followed by the high exposure category (7.1%) and the low exposure category (1.5%). The overall test and the medium versus low exposure contrast were significant ( $p=0.027$  and  $p=0.011$ , respectively). A marginal difference was detected in the high versus low exposure contrast ( $p=0.055$ ). Without the exposure index-by-race interaction in the model, significant differences were found ( $p=0.040$  for overall,  $p=0.040$  for medium vs. low, and  $p=0.033$  for high vs. low).

### Inclusion Cysts

Based on the adjusted and unadjusted analyses, no significant differences among the exposure categories were identified in the officer and enlisted flyer cohorts.

For the enlisted groundcrew cohort, no differences were detected among the exposure categories based on the unadjusted analysis. In the adjusted analysis, there was a significant exposure index-by-presence of pre-SEA acne interaction ( $p=0.005$ ). For the enlisted groundcrew with pre-SEA acne, the percentages with inclusion cysts were 6.1, 19.6, and 19.5 for the low, medium, and high exposure categories, respectively. For this stratum, the medium versus low contrast was significant ( $p=0.047$ ) and the high versus low contrast was marginally significant ( $p=0.088$ ). For the enlisted groundcrew without pre-SEA acne, the medium versus low exposure contrast was significant ( $p=0.025$ ), although this result did not support an increasing dose-response relationship (13.4% for low, 4.0% for medium, and 10.3% for high).

### Hyperpigmentation

No significant differences were found among the exposure categories in any of the occupational cohorts based on the unadjusted and adjusted analyses.

### Other Abnormalities

In the officer cohort, 77.7 percent in the low exposure category, 88.7 percent in the medium exposure category, and 78.4 percent in the high exposure category had at least one abnormality in the category of other dermatologic disorders. In the unadjusted analysis, the overall test and the medium versus low exposure contrast were significant ( $p=0.042$  and  $p=0.029$ , respectively). These findings were supported by the adjusted results ( $p=0.040$  for overall and  $p=0.049$  for medium vs. low). The high versus low exposure contrast was not significant in either the unadjusted or adjusted analysis.

The percentages of other abnormalities in the enlisted flyer cohort were 85.5, 69.8, and 86.8 in the low, medium, and high exposure categories, respectively. In the unadjusted analysis, the overall test was significant ( $p=0.036$ ) and the medium versus low exposure contrast was borderline significant ( $p=0.071$ ). After adjustment for covariates, both the overall test and the medium versus low exposure contrast were marginally significant ( $p=0.069$  and  $p=0.067$ , respectively). The high versus low contrast was not significant in the unadjusted and adjusted analyses.

No significant differences were detected in the enlisted groundcrew cohort in either the unadjusted or adjusted analyses.

### Dermatology Index

The dermatology index was dichotomized for the exposure index analyses: zero abnormalities versus at least one abnormality. The unadjusted exposure index analyses of the dermatology index did not reveal any significant differences among the exposure categories. These findings were supported by the results of the adjusted analyses for officers and enlisted flyers.

For the enlisted groundcrew, a significant exposure index-by-presence of pre-SEA acne interaction was present ( $p=0.025$ ). There were no significant differences among the exposure levels for participants without pre-SEA acne for the dermatology index. The percentage of participants classified as abnormal increased as exposure increased for participants with pre-SEA acne. Of the participants in the low exposure category, 36.7 percent were classified as abnormal. In the medium and high categories, the percentages of participants classified as abnormal were 46.4 and 53.7, respectively. The high versus low contrast was significant (Adj. RR: 2.10, 95% C.I.: [1.16, 3.81],  $p=0.014$ ). Without the exposure index-by-presence of pre-SEA acne interaction in the model, no significant differences among the exposure categories were identified.

### Longitudinal Analysis

The dermatology index was investigated to assess longitudinal differences between the Ranch Hand and Comparison groups. For this analysis, the index was dichotomized. Scores of 1 or greater were classified as abnormal, and a score of 0 was classified as normal. Table 14-10 summarizes the percentages of abnormal and normal scores for the 1982, 1985, and 1987 examinations. Table 14-11 presents a summary of the analysis comparing 1982 results with

TABLE 14-10.

**Summary Statistics for the Longitudinal Analysis of the  
Dermatology Index: 1982 Baseline, 1985 Followup,  
and 1987 Followup Examinations**

Examination	Statistic	Group			
		Ranch Hand		Comparison	
1982 Baseline	Number/%				
	Abnormal	350	38.3%	390	36.3%
	Normal	565	61.7%	684	63.7%
1985 Followup	Number/%				
	Abnormal	431	48.2%	518	49.0%
	Normal	464	51.8%	540	51.0%
1987 Followup	Number/%				
	Abnormal	355	38.8%	411	38.3%
	Normal	560	61.2%	663	61.7%

Note: Summary statistics for the 1982 Baseline and the 1987 followup are based on 915 Ranch Hands and 1,074 Comparisons who participated in the 1982 Baseline and the 1987 followup examinations. Summary statistics on 895 of these Ranch Hands and 1,058 of these Comparisons who also participated in the 1985 followup are also included for reference purposes only.

TABLE 14-11.

**Longitudinal Analysis of the Dermatology Index: A Contrast of 1982  
Baseline and 1987 Followup Examination Abnormalities**

Group	1982 Baseline Exam	1987 Followup Exam		Odds Ratio (OR)*	p-Value (OR <sub>RH</sub> vs. OR <sub>C</sub> )
		Abnormal	Normal		
Ranch Hand	Abnormal	189	161	1.03	0.648
	Normal	166	399		
Comparison	Abnormal	211	179	1.11	
	Normal	200	484		

\*Odds Ratio:  $\frac{\text{Number Normal Baseline, Abnormal 1987 Followup}}{\text{Number Abnormal Baseline, Normal 1987 Followup}}$

1987 results for each group. The results showed that the group difference did not change significantly over time for the dermatology index ( $p=0.648$ ).

## DISCUSSION

In any study of the biological effects of herbicides and their contaminants in humans, particular emphasis must be placed on the dermatologic examination. Of the organ systems subjected to analysis, only the skin has a clinical endpoint--chloracne--which has been conclusively related to dioxin exposure. Further, while the intact skin is a most effective protective barrier to even high concentrations of a wide range of industrial chemicals, it also serves, by cutaneous absorption, as a significant portal of entry through which internal organ systems are placed at risk of toxicity.

In dermatologic practice, as in all clinical disciplines, the history can be more important to accurate diagnosis than objective physical findings. This is particularly true in the case of chloracne which, apart from the characteristic cutaneous distribution, has no hallmark features that distinguish it from other more common acneiform eruptions. In the current study, examiners were strictly forbidden from taking any occupational history. Though at obvious variance with traditional practice, such restrictions were essential to the elimination of observer bias. During the examinations, dermatologists were instructed to biopsy lesions that were felt to be suspicious of skin cancer. Though blinded to the participants' herbicide exposure status, examiners performed a similar number of biopsies in the Ranch Hand (19) and Comparison (20) groups.

The rarity of chloracne is such that few dermatologists will encounter even a single case in a lifetime of practice. Experimental dose-response studies in animals and in humans have confirmed that the topical concentrations of TCDD required to produce overt lesions are far greater than that to which participants in the current study were likely to have been exposed in SEA. It is therefore not surprising that, in the three examination cycles completed to date, no active cases of chloracne have been detected. Recognizing the remote possibility that acute cases of chloracne may have occurred and resolved, several long-term complications of all forms of acne (scarring and hyperpigmentation) were included as dependent variables in comparative and longitudinal analyses. Neither of these complications of acne diseases were different in the two groups.

Most of the dependent variable-covariate associations documented in the current section would be expected in clinical practice. Though subject to considerable individual variation, age-related changes in the epidermis, stratum corneum, and corium are associated with thinning of the skin, an increase in capillary fragility, abnormalities in keratinization, dyshydrosis with wrinkling and scaling, and loss of elasticity. Hyperplasia of the epidermis is typically associated with keratoses (seborrheic and senile) and basal cell carcinomas.

Among the dermal appendages, the sebaceous glands typically become less active with age, though an increase in comedones in selected areas (often infraorbital and nasal) may occur. Also noted and present in various forms were pigmentation disorders. In association with atrophy of the skin,

depigmentation is common whereas with epidermal hyperplasia, hyperpigmentation can occur. With the exception of typical acne, which is more common at an early age, an increase in most other forms of skin disease would be expected over time and was documented in the current study.

Consistent with established clinical patterns, a number of skin diseases were found to occur more commonly in Black participants. As nonspecific sequelae to trauma or inflammation, hypo- and, more commonly, hyperpigmentation occur more frequently in dark skinned races. Acneiform lesions and, in fact, all follicular diseases occur more commonly in Blacks and may relate to race-specific variations in the shape and orientation of the hair follicles. Finally, as a genetically determined trait, exaggerated mesenchymal responses to trauma and inflammation are common in Blacks, with keloid formation being the most familiar example.

With one exception, group comparison of the variables analyzed revealed no significant differences between the Ranch Hands and Comparisons. As noted previously, close to an equal number of biopsies was performed in each group. The Ranch Hands were found to have a statistically significant increase in the incidence of post-SEA basal cell carcinoma, a finding that is discussed in Chapter 10, Malignancy. Though Ranch Hands were found to have a slightly greater incidence of reported acne developing after SEA service, the distribution of locations of acne was similar to that of the Comparisons and not in a pattern consistent with chloracne. This difference in reported acne was not corroborated on physical examination of the participants. Finally, longitudinal analysis of all cutaneous disorders over three examination cycles failed to reveal any health detriment related to group.

## SUMMARY

The 1987 dermatologic assessment was based on reported occurrence, duration, and location of acne; six dermatologic disorders: comedones, acneiform lesions, acneiform scars, depigmentation, inclusion cysts, and hyperpigmentation; other abnormalities; and a dermatology index based on the presence of comedones, acneiform lesions, acneiform scars, and inclusion cysts. Results of the Ranch Hand and Comparison contrasts are summarized in Table 14-12.

A significantly higher percentage of Ranch Hands than Comparisons reported that they had experienced at least one occurrence of acne during their lifetime ( $p=0.026$ ); the occurrence of acne in this analysis included episodes before the start of the first SEA tour. Subsequent analysis indicated that, for participants with no history of acne before the start of the first SEA tour, a higher percentage of Ranch Hands than Comparisons reported the occurrence of acne after the start of the first SEA tour ( $p=0.007$ ). No difference in the occurrence of acne after the start of the first SEA tour was present for participants with an occurrence of acne before the start of the first SEA tour. There was also no difference between the Ranch Hands and Comparisons based on the analysis of duration or location of acne, which was limited to participants with acne after the start of the first SEA tour. These observations suggest that the increased reports of acne after service in SEA were not due to chloracne.

TABLE 14-12.

**Overall Summary Results of Unadjusted and  
Adjusted Group Contrast Analyses of Dermatology Variables**

Variable	Type of Analysis	Unadjusted	Adjusted	Direction of Results
Occurrence of Acne				
Lifetime	D	0.026	--	RH>C
Relative to SEA Tour <sup>a</sup>				
Post-SEA vs. Pre-SEA/None		0.010	--	
Post-SEA/Pre- and Post-SEA				
vs. Pre-SEA/None		0.019	--	
Post-SEA vs. None		0.007	--	
Pre- and Post-SEA vs. Pre-SEA		NS	--	
Duration of Acne	C	NS	--	
Location of Acne	D	NS	--	
Comedones	D	NS	** (NS)	
Acneiform Lesions	D	NS	NS	
Acneiform Scars	D	NS	NS	
Depigmentation	D	NS	NS	
Inclusion Cysts	D	NS	NS	
Hyperpigmentation	D	NS	NS	
Other Abnormalities	D	NS	NS	
Dermatology Index	D	NS	NS	

D: Discrete analysis performed.

--Analysis not performed.

RH>C: Higher prevalence rate in Ranch Hands than in Comparisons.

<sup>a</sup>The analyses of occurrence of acne relative to SEA tour are contrasts resulting from the further classification of lifetime occurrence of acne.

NS: Not significant ( $p > 0.10$ ).

C: Continuous analysis performed.

\*\* (NS): Group-by-covariate interaction ( $0.01 < p < 0.05$ ); not significant when interaction is deleted; refer to Table K-2 for a detailed description of this interaction.

The results revealed no significant differences between the two groups based on the unadjusted and adjusted analyses of acneiform lesions, acneiform scars, depigmentation, inclusion cysts, hyperpigmentation, other abnormalities, and the dermatology index determined at the physical examination. In the unadjusted analysis of comedones, no significant difference between the Ranch Hands and Comparisons was found; however, there was a significant group-by-race interaction in the adjusted analysis ( $p=0.049$ ). Exploration of the interaction revealed that the Black Ranch Hands had a marginally higher prevalence rate of comedones than the Black Comparisons ( $p=0.083$ ). No difference was found for the nonblacks. Without the group-by-race interaction in the model, no significant difference between the two groups was found based on the prevalence of comedones. The fact that there were no differences in duration or location of reported acne subsequent to service in SEA and the lack of group differences in the physical examination strongly suggest that the increase in reported acne was not due to chloracne. This increase in reported skin disease could be due to differential reporting or wartime living conditions among study participants.

In the exposure index analyses, most of the results did not suggest an increasing dose-response relationship that was consistent across the three exposure levels. However, in the unadjusted analysis of depigmentation for the enlisted groundcrew cohort, borderline significant differences were identified that were consistent with an increasing dose-response relationship. In the adjusted analysis of depigmentation for this cohort, there was an exposure index-by-race interaction. Exploration of the interaction resulted in significant and marginally significant differences; however, the percentages were no longer consistently increasing with exposure level. In the officer cohort, the overall tests and medium versus low exposure contrasts were significant based on the analyses of other abnormalities; however, the high versus low contrasts were not significant. In the adjusted analysis of the dermatology index, a significant exposure index-by-presence of pre-SEA acne interaction was found in the enlisted groundcrew. The high versus low contrast was significant for participants with pre-SEA acne, and the percentage of participants classified as abnormal increased as exposure levels increased. Clarification of these exposure analyses must await the completion of the serum dioxin assays.

Based on the longitudinal analysis of the dermatology index, the difference between groups did not change significantly between the 1982 Baseline and the 1987 followup examinations.

In conclusion, no current cases of chloracne were diagnosed at the 1987 physical examination. Although more Ranch Hands reported having experienced at least one occurrence of acne in their lifetime, the remainder of the dermatologic evaluation showed that the two groups were similar.

## CHAPTER 14

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